

How Much Pain for Cardiac Gain?

Government exercise guidelines say that moderate activity spread throughout the day is enough. But some researchers say the science doesn't support that conclusion

For a nation of couch potatoes, the news seemed too good to be true. For years, the prescription for maintaining healthy hearts had been vigorous exercise—running, swimming, aerobic dancing—whatever it took to get the heart rate up and keep it there for 20 to 30 minutes at least three times a week. But in July 1993, that message changed.

A panel of exercise researchers convened by the Centers for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) reported that people needn't exercise vigorously to improve their health. The panel concluded that moderate levels of moderate activity—walking, housework, gardening, or playing with children—broken up over the course of the day, provide the bulk of exercise-related health benefits. "Still Don't Exercise? No Sweat," cooed one reassuring headline that followed; "A Little at a Time Now Called Enough."

Since then, the message conveyed by those first headlines has become official U.S. policy. The National Institutes of Health and the Surgeon General's office have weighed in with similar recommendations, as has the American Heart Association. But despite this apparent consensus, there is considerable disagreement in the exercise research community about whether the recommendations are amply supported by scientific data.

Policy-makers caught in the middle of this disagreement are in a difficult position. How they interpret the conflicting data could affect the lives of millions of people: Recommend too rigorous a regimen and people may be scared off; recommend easier goals and many may be deterred from getting the full benefits of harder exercise. It's a classic dilemma confronting health experts in areas ranging from mammography to diet, where the scientific data are not clear-cut.

The current guidelines "overemphasize the benefits of moderate exercise to make it more palatable to the public," says statistician and exercise researcher Paul Williams of the Lawrence Berkeley National Laboratory in Berkeley, California, the most vocal critic of the recommendations. He maintains that neither his own research nor a reanalysis of

the data on which the CDC/ACSM panel and other groups based their conclusions supports the idea that moderate amounts of activity confer the bulk of health benefits, nor do they support the argument that those moderate amounts can be equally effective when split into small blocks of time during the day.

Williams is not alone in his concerns. "I'm not convinced that the 'exercise-lite' routine really makes a difference," says cardiologist Paul Thompson of Hartford Hospital in Hartford, Connecticut. "There are very few solid data," he adds, to support the reports' recommendations for exercise amounts and intensities. Even some of the members of the CDC/ACSM panel have reservations about the final recommendations. "I suppose I should have produced a minority report," says epidemiologist Jeremy Morris, of the London School of Hygiene and Tropical Medicine in the United Kingdom. Morris signed the report, although his own studies

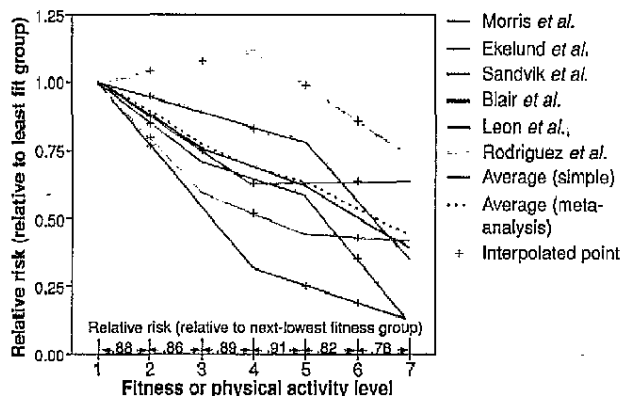
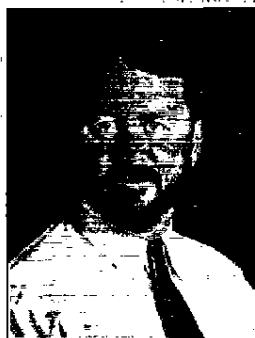
calls "considerable consistency" in epidemiological studies suggesting that moderate amounts of activity provide benefits. Another defender is University of Minnesota epidemiologist Arthur Leon, an author on the CDC and other consensus reports. He also directed the Multiple Risk Factors Intervention Trial (MRFIT), which looked at activity levels in its study of risk factors for heart disease in more than 12,000 men over a period of 7 years. Leon says that study suggests health benefits from moderate levels of activity, and "the [recommendation report] was based on the majority of studies saying the same thing."

This is no mere academic dispute. According to the CDC, inactivity contributes to more than a third of the nearly 500,000 annual heart-disease-related deaths in the United States. And policy-makers are desperate to find a way to get people to exercise. "The old message of 'burn, baby, burn,' to do 1 hour of vigorous activity three times a week, turned people off," says Leon. He and his co-authors hope the 1993 guidelines are less formidable and therefore have more effect.

Williams counters, however, that no psychological testing was done to see whether people would respond as expected to the recommendations. Critics also worry that even if the recommendations have the desired effect, they can't deliver the benefits they promise. "People who are thinking about exercising might get the impression that if they do just a little bit, they'll get all these wonderful benefits," says exercise researcher Peter Wood of Stanford Medical School. "The evidence does not support that." What's more, he adds, "people who are already doing substantially more [exercise] ... might get the impression that they are wasting their time," and quit beneficial exercise routines.

The moderation message

The notion that moderate levels of moderate activity could provide protection against heart disease came from large epidemio-



No diminishing returns. In the analysis by Paul Williams (upper left), heart-death risk (meta-analysis result, dashed red line; simple average, solid red line) dropped steadily as exercise increased. The black lines depict the results of the individual studies on which the analysis was based.

have concluded that sustained, vigorous activity is necessary to ward off heart disease.

Defenders of the guidelines say the data are sound enough to back their recommendations. "I stand by the conclusion that we made," says University of South Carolina exercise physiologist Russell Pate, former president of the ACSM and lead author on the CDC/ACSM report. He cites what he



Sovereignty threat? House bill would end U.S. role in UN "biosphere reserves" program.

Lawmakers Target Biosphere Program

Back when few people had heard of ideas like biodiversity and sustainable development, the United Nations set up a voluntary network of ecology research sites to explore ways to use natural resources without destroying them. But several House members claim the 29-year-old UN Man and the Biosphere (MAB) program impinges on the rights of property owners, and they want to pull the plug on U.S. participation.

MAB's 339 "biosphere reserves" include 47 sites in the United States, most of them national parks or wilderness areas. Each reserve comprises a core protected area and the adjacent land managed for uses such as recreation or forestry. The combination allows visiting researchers to do comparative studies, for instance, on minimizing the impact of tourism on biodiversity.

But Representative Don Young (R-AK) claims the re-

serves trample on citizens' rights by influencing nearby land-use decisions. Young's resources committee is considering a bill that would remove all 47 U.S. reserves from MAB in 3 years unless each one obtained congressional approval. A similar bill nearly passed the House last fall.

If the program is killed, says the Smithsonian Institution's Thomas Lovejoy, a former USMAB chair, "this inherently sensible scientific approach to resource management would be lost."

The reserves aren't the only worry for USMAB, run by the State Department: Representative Tom Coburn (R-OK) is leading an effort to kill the program's \$1.2 million budget, which comes from 14 federal agencies and also funds peer-reviewed research. This month, the House passed authorization bills that bar the National Science Foundation and NASA from funding MAB. Even if those bills don't become law, an aide for Coburn says he hopes to persuade spending committees to cut MAB money.

U.K. Revamps University Research Grants

Britain's Medical Research Council (MRC) is planning major changes in the way it funds projects in universities, pushing researchers to forge collaborations or else see their funds dry up.

The MRC, which now spends

\$110 million per year on short-term project grants and related projects to individual university scientists, plans to replace its old funding scheme with five new categories that will focus funding on multidisciplinary teams large enough to create a critical mass. At the core are two categories—Cooperative Group Grants and Centre Grants—which will fund about 100 teams. Another two categories will help universities and researchers build strengths to compete for group grants. A fifth category will continue to fund individual investigators with small grants, but only those with a proven track record.

The new categories, which begin in 1998, will cut administration costs by reducing the number of projects that undergo peer review. The present subject-based grant panels will be scrapped in favor of a single advisory board for initial scientific assessment of proposed projects. A second board will then examine how well the projects fit the new multidisciplinary mission.

The changes "allow universities both to build on existing research strengths and provide opportunities to develop expertise in new areas," an MRC spokesperson says. But the new plan poses a threat to funding for small single groups. As the spokesperson says: "They should think about getting themselves into a co-op."

Germany May Relax Genome Data Policy

Following a meeting in Bonn on 26 May, German science officials appear likely to defuse a dispute enveloping the country's new genome research program. According to Knut Bauer of the research ministry, a clause granting industrial contributors 3 months of exclusive access to sequence data before they are put on the Internet may soon be dropped, in favor of immediate release.

Such a decision would represent a victory for academic scientists. At a February meeting in Bermuda, researchers from the world's major sequencing centers strongly objected to the German policy, which they said violates the principle of immediate data release endorsed the year before by all participants (*Science*, 23 May, p. 1189). They also threatened to exclude Germany from their international genome collaboration.

The controversial policy was a response to what some experts see as more favorable patent laws in the United States. But now German leaders appear to have set their patent concerns aside. At the Bonn meeting, according to several participants, key genome scientists, industry representatives, and ministry officials agreed that the country must avoid a potentially disastrous conflict over data sharing. "Our top priority is to stay in the international scientific community in this field," says Bauer. And "elimination" of privileged access for industry looks like the best way, he says. This thinking was influenced in part by a talk last week with U.S. genome program chief Francis Collins, Bauer adds.

Andre Rosenthal, who coordinates Germany's planned genomic sequencing effort, left the meeting hopeful that the policy will be reversed. But he worries that the issue will arise again for other genomic data, such as cDNA sequences. "I think we might see this battle fought over and over," he warns.

Gingrich Proposes Biodiversity Year

House Speaker Newt Gingrich (R-GA), who favors grand strategies in politics, wants scientists to think big about biodiversity.

Speaking last week in Washington, D.C., at an international meeting on oceans and security, the Speaker challenged his audience to come up with a plan for an International Biodiversity Year (IBY) to study the planet's living systems. Gingrich compared the idea to the International Geophysical Year of 1958-59, a hugely successful collaboration to study Earth's physical features. "Be bold," he said, "push the envelope. ... It's our job [in Congress] to be practical."

The IBY concept, says an aide, stems from conversations with scientists about the gaps in our knowledge of Earth's species and the potential value of new products derived from nature. One of Gingrich's advisers, Cornell biologist Tom Eisner, calls it "a

useful concept for uniting disparate factions and raising consciousness" about the need for biodiversity research. Environmentalists see an IBY as a chance to jump-start other activities—for example, an international project called Diversitas, which Stanford biologist Hal Mooney describes as "a region-by-region survey of what we have and what we've lost," is targeted to begin in 2001. And Peter Raven, head of the Missouri Botanical Gardens, sees IBY as a useful prod for U.S. ratification of the 1992 Convention on Biodiversity.

Paying for IBY won't be easy in an era of tight budgets. "The first question my bosses would ask is, 'In lieu of what mandated program?'" says one federal research official. But when it comes to finding money for new ideas, it can't hurt to have a powerful advocate like the Speaker.

How Exercise Works Its Magic

Although researchers are arguing about how much exercise you need to reduce your risk of heart disease (see main text), there is no doubt that at some point, physical benefits do kick in. "Exercise has lots of different effects" that can help protect your heart, says cardiologist Paul Thompson of Hartford Hospital in Hartford, Connecticut. Among them: It lowers blood pressure, boosts blood volume, and consumes "bad" fats in the blood (such as triglycerides), while also raising levels of the so-called good cholesterol carried in the blood's high-density lipoprotein (HDL) particles.

One of the best documented effects of exercise is on blood pressure. Even a single bout of moderate exercise can help. In a 1991 study, for example, Linda Pescatello, at the University of Hartford in Connecticut, found that blood pressure reductions of 6 to 10 millimeters of mercury could be detected immediately after hypertensive men bicycled at a moderate level (less than half the total intensity they were capable of) for 30 minutes. What's more, the reductions lasted for up to 13 hours. Exercise decreases blood pressure at least in part by turning down the activity of the sympathetic nervous system, which in turn relaxes the tension in artery walls, says physiologist Ethan Nadel of the Yale University School of Medicine.

Exercise not only lowers the pressure in arterial vessels, it also increases the volume of blood coursing through the entire vascular system. Thompson injected tracer substances into the bloodstreams of highly fit male distance runners; using the resulting concentration of the tracer to determine blood volume, he found that runners have nearly a liter more blood than average men.

As in the case of blood pressure, some of this effect can be seen immediately. Nadel found that one exercise session will raise blood volume, although the subjects had to exercise for 30 minutes at 80% of their maximal aerobic power, an exercise intensity

"at which you feel winded," says Nadel. Exercise causes the surge in blood volume by turning down the sensitivity of the volume-control system: a sensor in the right chamber of the heart that monitors blood volume and tells the kidneys to remove fluid when that volume gets high.

An expanded blood volume has multiple benefits, says Nadel. It boosts the volume of blood that fills the heart between contractions and thus the amount of blood the heart pumps with each stroke. "That makes the heart pump more efficiently," he says, and

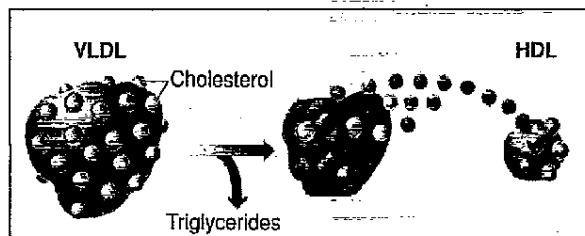
contributes to the characteristic low resting heart rates of athletes. The extra blood volume also dilutes bad actors in the blood, such as lipids that can produce fatty deposits on blood-vessel walls. "If [your blood is] dilute, it is less likely that cholesterol will bump up against your artery wall," says Thompson.

But a workout does more to the fats in your blood than simply dilute them: It directly changes them as well. High blood concentrations

of triglyceride fats have been linked to an increased risk of heart attack, and exercise reduces blood triglyceride levels. One way it does so, Thompson says, is by making muscles "hungry for fat." To satisfy their hunger, the muscles crank up an enzyme called lipoprotein lipase (LPL), which chews up triglycerides for the muscles to use as fuel. The weight loss associated with regular exercise also raises LPL activity in fat cells.

This increased LPL activity leads to another benefit: It helps to reduce blood cholesterol. As triglycerides are consumed, there is shrinkage of the very low density lipoprotein particles (VLDL), which store the fat in the blood. This causes some of the cholesterol stored on their surface to be jettisoned and picked up by the HDLs, which modify the cholesterol and deliver some of it to the liver for elimination from the body. Which of these many different effects is most significant for cardiac health is not clear, Thompson says, but together "they add up to a lot."

—M.B.



Jumping ship. Exercise drains triglyceride molecules from the core of very low density lipoprotein (VLDL) particles, forcing cholesterol to leave the particles' shrinking surface and be picked up by high-density lipoprotein (HDL) particles.

logical studies. In one of these, epidemiologist Ralph Paffenbarger of Stanford Medical School and his colleagues surveyed nearly 17,000 male Harvard alumni, aged 35 to 74. The subjects filled out a questionnaire about their regular physical activities; the researchers then tracked them for 12 to 16 years, logging heart attacks and deaths. They found that men whose reported activities burned more than 2000 kilocalories (kcal) per week—which can be done with a brisk daily walk of 45 minutes or so—had a 28% lower death rate than those who burned fewer calories.

A different type of study, conducted by Steven Blair at the Cooper Institute for Aerobics Research in Dallas, came to a similar conclusion. Based on their performances on a treadmill test, Blair assigned

more than 10,000 men and 3000 women to fitness categories, which his work had shown to reflect, roughly, a person's level of physical activity. Blair found that the least fit 20% of his subjects were most likely to die over the 8-year course of his study, and that the greatest reduction in the risk of death was between the least fit and the next-highest category. Other studies have shown that regular exercise raises a person's fitness level, and Blair concluded that even moderate activity such as a brisk daily walk would be enough to lift the least fit out of their high-risk status.

Blair's methods have been somewhat controversial because fitness is influenced by genetics as well as by activity level. Moreover, Williams urges caution in using a study that measures fitness but not activity to sup-

port recommendations for the activity levels necessary for health. "If you are making recommendations on physical activity, it seems to me you should emphasize studies that measure physical activity," says Williams.

Nevertheless, when Blair's results were considered along with Paffenbarger's and those from other large studies based on activity questionnaires, the collective impression was, says Blair, that "you get considerable protection from moderate amounts and intensities of exercise." While the studies suggested that more activity produced additional benefit, he says, the returns appeared to diminish at higher levels of exercise. These conclusions became the centerpiece of the CDC/ACSM consensus report and subsequent reports as well.

But Williams, who was not part of any of

the panels that produced those reports, takes issue with the claim that moderate amounts of activity—amounts that would burn just a couple of hundred kcal a day—provide the bulk of the protection against heart disease. Even the studies cited in the consensus report don't support that claim, he says. Williams subjected the data in those studies, plus some from a similarly designed study published after the report, to a statistical technique known as meta-analysis, which allows the averaging of data from multiple studies. He did not find the initial benefits from exercise followed by diminishing, as the report claims, but instead a linear decline in the risk of dying from heart disease. "This argues that there isn't the dose-response relationship the government is putting forward," he says.

What's more, Williams's own studies, reported in the past year, suggest that the benefits of exercise keep accruing linearly up to quite high levels of exercise. He related heart-risk indicators, such as HDL cholesterol levels, to miles run per week in 10,000 male and female runners whom he recruited at races and through ads in *Runner's World* magazine. After controlling for some differences in lifestyle, such as diet and smoking, he found that the risk factors improve linearly with the runners' weekly mileage up to 40 to 50 miles per week, a result suggesting that their risk of heart disease declined as their exercise level increased. Those runners were expending up to 5500 kcal a week, compared to the mere 1500 kcal a week recommended by the guidelines. The fact that they still saw linear increases in benefits at the upper end of that range makes it impossible, Williams says, for the report to be correct in saying that the preponderance of benefits comes from expending 1500 kcal/week.

Other researchers question whether Williams's findings with runners can be extended to the general public. "Paul found that runners who run a marathon were better off than runners who run half a marathon," scoffs Minnesota's Leon. "I don't think that pertains to too many Americans." What's

more, says Leon, the MRFIT study suggested that vigorous exercise may actually increase the risk of a heart attack in sedentary men who have a high risk of heart disease.

Blair suggests that Williams is comparing apples and oranges when he contrasts his findings on risk factors such as blood lipid concentrations to the consensus report's conclusions, which relied on heart attacks and deaths. "I don't think it is impossible to have a [linear] dose-response relation between running and the risk factors that he looked at," says Blair. But, he adds, that doesn't mean such a relation will translate into proportionally reduced death rates.

In addition to Williams's arguments over the quantity of calories that must be spent for the most benefit, there is another debate simmering over the manner in which

those calories are spent—in vigorous or just moderate exercise. The guidelines say the exercise need be only of moderate intensity—which generally means not intense enough to make you feel winded or break into a sweat from the exertion. Indeed, the recommended activities include mowing the lawn with a power mower or painting the house.

But even some of the members of the original CDC panel don't agree with that part of the recommendation. For example, London's Morris studied roughly 28,000 male British civil servants who filled out questionnaires about their leisure-time activities. He found that only those who regularly performed sustained vigorous activities, such as jogging, swimming, cycling, or vigorous sports, such as refereeing soccer matches, showed reduced risks of heart attacks. "We found very little benefit

with what we called recreational work: gardening, working on the car, working around the house," says Morris.

Nor, added Morris, was there any benefit from "ordinary walking"; only those who reported walking at the vigorous rate of more than 4 miles per hour saw significant benefits. Similarly, Harvard exercise researcher I-Min Lee, a collaborator with Paffenbarger,

did a recent analysis of the Harvard alumni data, from which she concluded that exercise had to be vigorous to protect against heart attacks. But Lee points out that she grouped moderate with light exercise as "nonvigorous" activity, raising the possibility that including the less active subjects may have masked any protective effects conferred by moderate exercise. She plans to address that issue in future work.

Minnesota's Leon says the flaw in Morris and Lee's studies was their classification of swimming and brisk walking as "vigorous." Leon contends that they are "moderate"; if Morris and Lee had classified them as such, he says, they might have found moderate exercise to be beneficial after all.

Researchers on both sides of the argument acknowledge that exercise intensity is a continuum, with brisk walking and swimming close to the border between moderate and vigorous activity. But Williams says brisk walking is at the vigorous end of what the government guidelines suggest. "If you look at the list [of recommended activities], you are talking about home care, playing with your children ... there is a lot more at issue here than just walking briskly." Pate points out that the recommendations suggest that activities other than walking should be of an intensity similar to a brisk walk at 3 to 4 miles an hour.

Breaking it up

Beyond the issue of intensity is the perhaps more crucial question of whether exercise must be done for a sustained time to be effective, or whether it can be broken up into short bouts with equal benefit. Many of the activities suggested by the guidelines, such as cleaning the house or taking the stairs rather than the elevator, are not done in the sustained way that intentional exercise is. Blair says that's irrelevant: "If you spend 200 [kilo]calories a day, you get 200 [kilo]calories worth of benefits. It doesn't matter very much if you get that all at one time, whether you get it from moderate or high intensity, or if it is discontinuous." The evidence for that view, he says, comes in part from epidemiological studies such as those by Paffenbarger, Morris, and MRFIT. Pate agrees: "If you look at how the activity is measured and reported in those studies, I think you would be hard pressed to conclude that what people are reporting is for the most part prolonged and continuous activity."

But the authors of some of the studies disagree. "The word 'sustained' is important," says Paffenbarger, noting what his own work showed: Among men who expended the same amount of calories weekly those who did some form of sustained exercise had significantly lower death and heart attack rates than those who didn't. Like-



Walk, don't run? How much you need to exercise on a treadmill—or elsewhere—is at the heart of the current debate.



Moderation pays. Studies by Steven Blair (above) suggest that even moderate exercise helps.

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wise, Morris says the activities that provided protection from heart attacks to the men in his study were those typically done for a sustained time, such as swimming, bicycling, or playing a sport. "Our men just didn't [break up their exercise]," Morris points out. "By the time a middle-aged man swims on the way to his office or on his way home, for the sake of his health, he swims for a reasonable time."

But there is also nonepidemiological evidence that exercise can be broken up, says Pate. The consensus reports cite two small studies in which subjects were assigned to exercise for 30 minutes a day—either in one stretch, or in two or three bouts of 15 or 10 minutes—for a period of 8 to 10 weeks. Both studies showed improvements in fitness, as determined by treadmill or equivalent tests. But they did not demonstrate that the improved fitness paid off in improved cardiac risk factors. And, as Williams notes, neither

was a true test of moderate exercise: One specified running; the other included jogging. "You seem to get the same effects [on fitness] with smaller bouts as with a single bout," says Williams, "but that doesn't imply the same will be true for intermittent bouts of moderate activity affecting risk of heart disease." Paffenbarger, who was an author of the CDC/ACSM guidelines, agrees with Williams. "There are no data to indicate that three short bouts of activity are equivalent to one large bout in terms of reducing disease risk, disease incidence, or mortality," he says. "That is a guess that is built into the CDC guidelines."

Supporters of the guidelines say that acting on a few such guesses is justified, given the public health stakes. They note that the Surgeon General's report is more carefully stacked with caveats than the earlier CDC/ACSM report was. It points out repeatedly, for example, that additional ben-

efits can be gained by more activity, and it soft-pedals the issue of breaking up exercise with the statement that "strictly speaking, the health benefits of such intermittent activity have not yet been demonstrated."

To remove some of the guesswork from future recommendations, Thompson and others advocate balancing the epidemiological studies with more trials in which subjects are placed on specific exercise regimens, to answer questions about intensity, duration, and amounts of exercise necessary to produce specific results. While we wait for these results, Pate pleads that we "not obscure the big conclusion here, which is that we are paying an enormous public health cost for our sedentary lifestyle in this country. We have an awful lot of very inactive people. I don't hear anybody saying [that we should] just leave them where they are while we settle this."

—Marcia Barinaga

ASTHMA GENETICS

A Scientific Result Without the Science

In the old days—say, 2 or 3 years ago—breakthroughs in basic research were almost always unannounced at scientific meetings or published in peer-reviewed journals. No longer. Last week, Sequana Therapeutics Inc., in San Diego, issued a press release declaring that the company had "discovered a gene responsible for asthma." The three-page release contained little data of use to other researchers—such as here the gene is located, what it might do, or how many sufferers might carry it. Nor is anyone likely to find the answers in journals or at meetings anytime soon. Sequana and its collaborators are in "the very early stages" of preparing a manuscript describing the finding, says geneticist Mary K. McCormick, head of Sequana's asthma division. She says it might be published "within a year."

The reason Sequana preempted the traditional scientific publication process has little to do with science. The announcement alerted investors that the discovery will earn the company a \$2 million "milestone payment" from Sequana's collaborator, pharmaceutical giant Boehringer Ingelheim. Indeed, Sequana's stock rose from \$13½ to \$14 the day after the announcement. And if the company had kept the news to itself, its employees and collaborators would risk insider-trading charges if they bought or sold Sequana stock, says company CEO Kevin Kinsella. At the same time, Sequana does not want to disclose details until it has filed for a patent and given Boehringer Ingelheim "some lead time" to develop treatments based on the gene, says Sequana's chief scientist, Tim Harris.

Sequana isn't the only biotechnology company to announce a major basic re-

search finding by press release. Last November, Cambridge, Massachusetts-based Millennium Pharmaceuticals claimed that it had found a diabetes gene, and in January, Salt Lake City-based Myriad Genetics announced that its researchers had bagged a gene linked to a type of brain cancer—both without scientific specifics (*Science*, 28 March, p. 1876). And these surely won't be the last such announcements: "I'm not a fan of genetics by press release," says Harris, "but it's an inevitable part of life at a biotech company that finds genes for a living."

It's becoming a part of life in academic genetics, as well. Untangling the complicated genetics of diseases such as diabetes or asthma "is very expensive research," says geneticist William Cookson of Oxford University. "It is difficult to imagine all the loci being identified without some commercial funding." One of Sequana's academic collaborators, pulmonologist Arthur Slutsky of the University of Toronto, agrees. Boehringer Ingelheim and Sequana have spent more than \$10 million to find this gene—more than the Canadian government has spent on the entire human genome project in the last 2 years, he says. But the

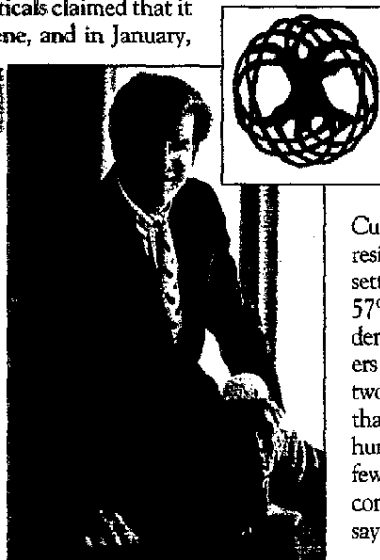
price for that support is the secrecy imposed by for-profit funding sources, says Cookson.

Sequana's results have been eagerly anticipated. The Toronto group, including Slutsky and Noe Zamel, published a paper last June in the *American Journal of Respiratory and Critical Care Medicine* describing their work with the residents of the South Atlantic island of Tristan da

Cunha. Most of the nearly 300 residents are descendants of 15 settlers from the early 1800s, and 57% have at least partial evidence of asthma. The researchers later said that they had found two chromosomal linkages, and that one was narrowed to a few hundred thousand base pairs. "A few weeks ago," the team was confident enough of their data to say they had a gene, says Slutsky.

The press release quotes pediatrician Richard O'Connor of the University of California, San Diego, as saying the discovery is "this century's most important finding in the etiology of asthma." But other researchers are less exuberant. "It is unlikely that this is the major genetic effect in asthma," says Cookson, who, with others, has found several chromosomal linkages to allergy and asthma. "It's definitely an impressive piece of science," he says, but until a more traditional scientific announcement is made "its overall value is impossible to judge." That judgment is months away. Don't hold your breath.

—Gretchen Vogel



Genetics by press release. Kevin Kinsella, with Sequana logo.

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NRC Lets a Little Sun Shine In

Change is hard for any organization, but officials at the National Research Council (NRC) have decided that, if it is inevitable, they'd rather be calling the shots. Faced with the prospect that the courts eventually could force it to abide by strict government rules on openness, the council recently approved new guidelines intended to open its inner workings "to the greatest extent possible." But the new rules fall far short of the government rules, and they appear unlikely to quiet critics.

The new policy has been in the works for more than a year at the NRC—the operating arm of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine that produces authoritative reports for those who make public policy (*Science*, 9 May, p. 900). But progress toward openness had been slowed by internal dissent. Early this year, however, environmental and animal-rights groups scored victories in two court cases that challenge the traditional secrecy with which the council does business (*Science*, 17 January, p. 297).

The groups want the NRC to abide by the Federal Advisory Committee Act (FACA), which specifies policies that government agencies using outside counsel must follow to ensure public input. In one case, a federal court refused to allow the U.S. Department of Energy to use an NRC report it requested; in another, the court has agreed that the council should have abided by FACA in conducting an animal case study for the National Institutes of Health. NRC officials intend to appeal the latter case to the Supreme Court, says Executive Officer William Colglazier. The officials worry that the cases might end with a ruling forcing them to adhere to FACA.

Given these external threats, "this time there was very little opposition" to the openness guidelines, says Colglazier. The council's governing board adopted the measures on 14 May.

Until now, meetings to discuss or prepare NRC reports typically were closed to all but committee members and staff. The rationale was that publicity could damage the institution's reputation for independence and fairness. The new policy, however, says that the council's work "can benefit from increased public access and increased opportunities for public input" at those meetings in which panel members are gathering information. That openness must be balanced by assurances that "committees and panels are shielded from undue pressures."

"The institution retains the right to close meetings as appropriate," the policy states,

"to conduct work free from external influences." But Colglazier says there must be compelling reasons for a committee to operate in private. "We will make it extremely rare that information-gathering meetings are closed," he says. Panel members also will be expected to discuss their potential biases during an open session at the start of their work.

The policy went into effect immediately. Last week, the NRC set up a World Wide Web site to provide up to 2 months' notice of open meetings (www2.nas.edu/whatsnew/events.html).

While the new rules reflect a major change from past practices, they fall far short of the FACA requirements. Under that law, all ses-

sions of advisory panels must be open, unless they involve classified or proprietary material or personnel matters. Agency chiefs cannot overrule the law, although federal advisory committees often skirt the rules by holding closed-door executive sessions.

Colglazier says the new rules are not designed to placate the courts or critics, but he hopes they "will buy us some goodwill" among opponents. However, that might be wishful thinking. "The effect [of the new policy] is minimal," says Valerie Stanley, legal counsel for the Animal Legal Defense Fund, which is suing the National Institutes of Health over its sponsorship of an NRC study on animal protection that followed the usual council procedures. "The meetings in which they set policy won't be open, and that's at the heart of what they do."

—Andrew Lawler

1998 BUDGET



Five-Year Plan Squeezes R&D

The dust surrounding the historic budget agreement between the Administration and Congress is starting to settle, and the emerging picture is not a pretty one for science and technology spending. A long-term budget plan based on that agreement was approved last week by the House and Senate, and it leaves no room for an R&D funding increase in the next 5 years. While the projections are far from immutable, they are raising concerns among R&D supporters in Congress.

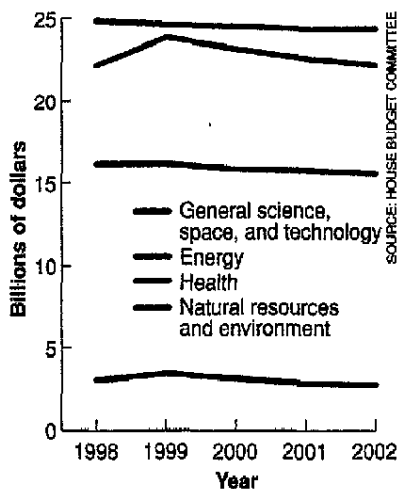
The budget resolution, which sets broad spending guidelines for the next 5 years, is the result of a bipartisan attempt by President Bill Clinton and Republican leaders to cut taxes and eliminate the federal deficit by 2002. That political consensus makes the resolution a more significant document than previous versions, which were based on one party's view of the future. And its message to scientists is that civilian R&D does not fare well. "They protected a lot of things, but R&D was not one of them," says Al Teich, science policy director at the American Association for the Advancement of Science (AAAS, which publishes *Science*). Of course, such projections are notoriously changeable, and the appropriators who actually allot program funding have

substantial freedom each year to fund what they see fit.

If the numbers in the resolution come to pass, warns House Science Committee Chair James Sensenbrenner (R-WI), "we'll be spending less in 2002 on scientific research ... than we did in 1991" after taking inflation into account. That reduction is the result of a decision to erase the deficit largely by reducing domestic discretionary spending, the account which includes all civilian science and technology. The budget resolution calls for a freeze or slight decrease in most R&D-related accounts as part of that effort. The only R&D-related area that the Administration and Congress singled out to protect is the Commerce Department's National Institute of Standards and Technology, which oversees the controversial Advanced Technology Program. ATP has been the object of a tug-of-war between

some Republicans, who see it as corporate welfare, and the president, who regards it as a vital link between government and industry.

Funding for the natural sciences, including research at NASA, the National Science Foundation, and physics programs within the Department of Energy (DOE), would take a "pretty significant hit" under the plan, says Sensenbrenner, who told a recent meeting of science writers that he was "dismayed" by the numbers



Flat-lined. R&D doesn't even keep up with inflation in the budget resolution.